PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Keiya Ozawa et al.	Art Unit:	1634
Serial No.:	09/905,591	Examiner:	B. Sisson
Filed:	July 13, 2001	Customer No.:	21559
Title:	METHOD FOR CAUSING SELECTIVE PROLIFERATION OF A CELL (As Amended)		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF DR. YASUJI UEDA

I declare:

1. I am an inventor of the above-referenced application, and I am currently an Assistant Professor at Chiba University Graduate School of Medicine.

2. I am also an author of Hara et al. ("Expansion of Genetically Corrected Neutrophils in Chronic Granulomatous Disease Mice by Cotransferring a Therapeutic Gene and a Selective Amplifier Gene," Gene Therapy 11:1370-1377, 2004; "the Hara et al. publication;" copy enclosed as Exhibit 1).

3. The Hara et al. publication describes *in vivo* selective proliferation of bone marrow cells transduced with a construct (MGK/h91GE) encoding a chimeric protein having a granulocyte colony stimulating factor receptor extracellular domain with amino acids 5-195

deleted and a phenylalanine substitution for tyrosine 703 and an intracellular domain including an estrogen receptor hormone binding domain. The MGK/h91GE construct also contains $gp91^{phox}$ (a desired exogenous gene encoding the NADPH oxidase $gp91^{phox}$ subunit).

4. Estrogen was administered to a cohort of the transplants and neutrophil superoxidase production was monitored. A significant increase in oxidase-positive cells was observed in the estrogen-treated mice, and repeated estrogen administration maintained the elevation of transduced cells for twenty weeks. Moreover, oxidase-positive neutrophils were increased in the transplants given the first estrogen at nine months post-transplantation.

5. The results presented in the Hara et al. publication indicate that transduced long-term repopulating cells expressing a fusion protein containing a granulocyte colony stimulating factor receptor extracellular portion and an estrogen receptor hormone binding domain intracellular portion were maintained *in vivo* and selectively proliferated in response to estrogen stimulation.

6. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

March 15, 2006
Date

DR. YASUJI UEDA